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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,939	12/20/2000	Cesare Galli	P66004USO	8697

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,939	GALLI ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/14/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's election without traverse of group II, claims 19-21, in the reply filed on April 27, 2006 is acknowledged.

Claims 13-18 and 22-25 are withdrawn from consideration.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification does not disclose re-cloning by isolation of fetal fibroblasts, and using those cells as nuclear donor, not genetically modified or genetically modified, in a re-cloning method. This is the subject matter of claims 20 and 21.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 19-21 are to a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal to a suitable recipient and transferring a cell from the first generation embryo of a suit a suitable recipient to form a second generation embryo, and a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal to a suitable recipient, preparing fetal fibroblast cultures from the first generation embryo and transferring cells from said fetal fibroblast cultures to

a suitable recipient to form a second generation embryo, and where the fetal fibroblasts are genetically modified.

Claims 19-21 are not enabled because at the time of filing, the art regarded nuclear transfer, using a lymphocyte or leukocyte to be unpredictable. Galli teaches the production of one calf by repeat nuclear transfer, where the original nucleus was isolated from peripheral blood leukocytes (page 166, col. 1, lines 10-14). Repeat nuclear transfer, as disclosed in Galli, is the formation of an initial reconstructed embryo, isolating a blastomere from the resulting morulae, and transferring the blastomere into an enucleated MII oocyte (page 163, col. 1, parag. 3, to col. 2, lines 16). Galli states for successful nuclear transfer 2 steps in their protocol are essential: precise optimization of the size of the pipette and use of a piezostepper to rupture the oocyte membrane prior to nuclear injection (page 168, col. 1, parag. 1, lines 11-17). With mice, at the time of filing, nuclear transfer using nuclei from leukocytes and lymphocytes failed to produce mice (page 382, col. 2, parag. 1, lines 1-3 and 5-8; and page 380, Table 3). Wakayama states this result maybe due to gene rearrangement in lymphocytes, where some genes are poorly or not expressed because of the rearranged genome (page 382, col. 2, parag. 1, lines 13-17). Hochedlinger teaches the production of mice by nuclear transfer using B- and T-cell nuclei as nuclear donor by a two-step procedure where ES cells were derived from cloned blastocyst and injection of the ES cell into a tetraploid host blastocyst (page 1035, col. 1, parag. 2, lines 3-8). Hochedlinger supports statements made by Wakayama in stating reprogramming B- and T-cell nuclei are less efficient (page 1037, col. 2, parag. 2, lines 11-14). Claims 19-21 lack enablement because lymphocyte nuclei were regarded by the art as not contributing to the development of an animal by nuclear transfer without particular methodologies not disclosed in the specification. Thus, to make the claimed invention, the skilled artisan would have needed additional method steps not disclosed, and thus would have been required to make essential

steps before achieving animal production from lymphocyte nuclear donors. Therefore, it would have been regarded as unpredictable to produce a human or nonhuman animal using B- or T-cell as nuclear donors at the time of filing.

In addition, claims 19-21 are not enabled because at the time of filing, the art regarded the production of nonprimate mammals by nuclear transfer as not enabled. The cloning of monkeys by nuclear transfer had been successful when embryonic cells were the nuclear donors, not when somatic cells were used as nuclear donor (Mitalipov, abstract). Mitalipov further states, clearly, that somatic cell cloning, as is part of the present methods, has not been accomplished in primates (Mitalipov, page 1367, col. 2, parag, 3, lines 1-3). Simerly, states that in rhesus monkey NT units, DNA and microtubule imaging showed disarrayed mitotic spindles with misaligned chromosomes, which resulted in unequal chromosome segregation and aneuploid embryos (page 297, col. 2, parag. 1, lines 5-11). The art, therefore, at the time of filing clearly disclosed the unpredictable nature of nuclear transfer using a primate somatic cell as nuclear donor.

With regards to the method of nuclear transfer or method of cloning, the art at the time of filing only taught MII oocytes as cytoplast recipients. Only MII oocytes were regarded by the art has having the necessary components to reprogram or restructure a somatic cell genome to permit development. Campbell states MII arrested oocytes support the development of livestock species, cow and pig in particular, by nuclear transfer methods, where pronuclear zygotes as cytoplast reciepient do not (Campbell, page 246, col. 1, lines 22-25). The reasoning is the enucleation step when pronuclear zygotes are recipient cells in nuclear transfer removes factors essential in development (page 246, col. 1, lines 14-18). Further, MII oocytes contain high levels of MPF activity, necessary for nuclear envelope breakdown, chromosome condensation and other cytoskeletal changes associated with cell division (Campbell, page 246, col. 2, lines 7-17). Thus at the time of the present

invention (1998), the art regarded MII oocytes as the recipient cytoplast in nuclear transfer methods. The specification does not provide guidance for the use of any other recipient cytoplast that overcomes these teachings.

Therefore, at the time of filing, the skilled artisan would have needed to conduct an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: (claims 19-21) activation of the reconstructed embryo, culturing the activated reconstructed embryo to produce a first generation embryo and (claims 20-21) transferring the activated reconstructed embryo to a female, and permitting the embryo to develop into a fetus.

The claims are free of the prior art. At the time of filing the prior art did not teach or suggest a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal to a suitable recipient and transferring a cell from the first generation embryo of a suit a suitable recipient to form a second generation embryo, and a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal to a suitable recipient, preparing fetal fibroblast cultures from the first generation

embryo and transferring cells from said fetal fibroblast cultures to a suitable recipient to form a second generation embryo, and where the fetal fibroblasts are genetically modified.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

May 23, 2006